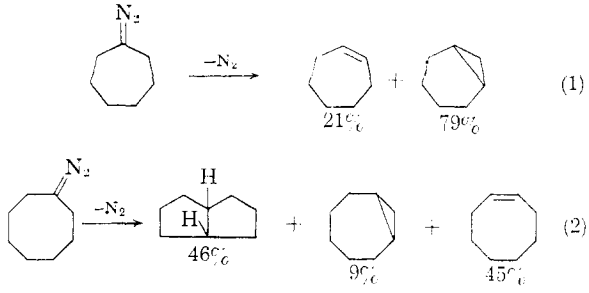
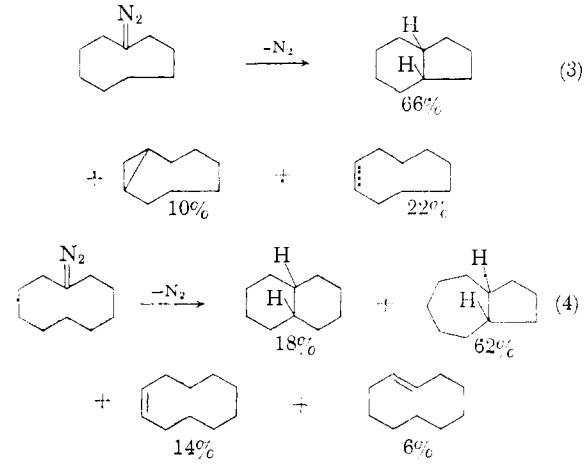
conversions of 2-diazocamphane and 2-diazonorbornane to tricyclene and nortricyclene, respectively. These results illustrate the differences in carbenic reactions of 6-membered rings in their chair and rigid-boat forms.

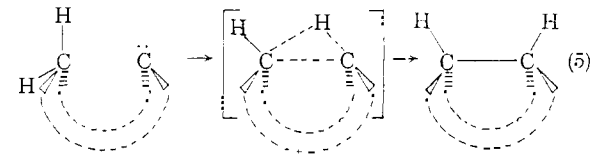
Decomposition of diazocycloheptane[6] (Equation 1) yielded bicyclo[4.1.0]heptane (18%) by 1,3-transannular insertion and cycloheptene (82%) by 1,2-rearrangement of hydrogen. Thermolysis of diazocycloöctane[6] (Equation 2) gave *cis*-bicyclo[3.3.0]octane (46%), bicyclo[5.1.0]octane (9%)[7] and *cis*-cycloöctene (45%). Diazocyclononane[8] (Equation 3) yielded *cis*-hydrindane (66%), bicyclo-



[6.1.0]nonane[9] (10%), and *cis*-cyclononene (22%). Diazocyclodecane[3] (Equation 4) gave a greater variety of transannular reactions than its lower homologs: *cis*-bicyclo[5.3.0]decane (62%) and *cis*-decalin (18%)[10] result from transannular insertion and *cis*-cyclodecene (14%) and *trans*-cyclodecene (6%) are formed by hydrogen rearrangement.



Carbenoid decomposition of C_7 through C_{10} diazocycloalkanes is thus characterized by extensive 1,3-, 1,5- and 1,6-transannular insertion along with rearrangement of α-hydrogen. It also is apparent that bicyclic products are formed much more efficiently by carbenic rather than cationic insertion processes.[5,11] The absence of 1,4-insertion products presumably stems from improper stereochemistry during decomposition of the medium-sized diazocycloalkanes. It is of interest that the insertion processes are stereoselective in that only *cis*-bicyclic hydrocarbons are formed. The extensive transannular insertion and the stereochemistry of decomposition of the diazocycloalkanes thus parallel reactions of lithium diethylamide with *cis*-cyclodecene oxide and *cis*-cycloöctene oxide to give *cis-cis*-1-decalol and *endo-cis*-bicyclo[5.3.0]decan-2-ol, and *endo-cis*-bicyclo[3.3.0]octane-2-ol, respectively, by processes involving simultaneous α-elimination and carbenic insertion.[12] The stereospecific transannular insertions of carbenic systems to give *cis*-bicyclic derivatives is a necessary consequence of transfer of axial hydrogen in ring systems (Equation 5[13a−c]) and is consistent with the principle that carbenic insertions occur with retention in configuration.[13d]



(7) Also prepared from cycloheptene, methylene iodide and zinc–copper: b.p. 141.5–142° (760 mm.), $n^{25}D$ 1.4601 (analytical sample).

(8) Essentially identical results have been obtained independently by A. C. Cope, M. Brown and G. L. Woo for decomposition of *p*-tosylhydrazones of cycloöctanone and cyclodecanone and will be reported separately by them. A preliminary account of this work was given by A. C. Cope in a lecture at the Robert A. Welch Foundation Conferences on Chemical Research in Houston, Texas, November 7, 1960.

(9) Also synthesized from *cis*-cycloöctene, methylene iodide and zinc–copper: b.p. 43° (8 mm.), $n^{25}D$ 1.4622 (analytical sample).

(10) A saturated hydrocarbon also was obtained (~1%) which has been assigned tentatively as bicyclo[7.1.0]decane.

(11) In base-catalyzed decomposition of C_7–C_{10} cycloalkanone tosylhydrazones in protonic solvents, processes which are in part cationic, the ratios of olefin to bicyclic products are considerably greater than those obtained from reactions under optimum carbenic conditions.

(12) (a) A. C. Cope, G. A. Berchtold, P. E. Peterson and S. H. Sharman, *J. Am. Chem. Soc.*, **82**, 6370 (1960). (b) Reactions of lithium diethylamide with *trans*-cyclodecene oxide and *trans*-cycloöctene oxide, presumably α-elimination carbenic processes, yield *cis trans*-1-decalol and *exo-cis*-bicyclo[3.3.0]octan-2-ol, respectively: A. C. Cope, M. Brown and H. H. Lee, *ibid.*, **80**, 2855 (1958), and A. C. Cope, H. H. Lee and H. E. Petree, *ibid.*, **80**, 2849 (1958).

(13) (a) On the basis of stereochemical criteria, it is also expected that the bicyclic products of kinetic control produced from transannular reactions of monocyclic derivatives via alkylation of the carbonium ion type or by nucleophilic displacement will be of *cis*-structure. (b) Formolysis of *trans*-cyclodecene oxide is reported to yield *trans*-1-decalol, m.p. 93°, as a transannular product. D. J. Cram in M. S. Newman's "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 286, suggests that the product is *trans-trans*-1-decalol. The present authors assign the structure of the transannular product as *cis-cis*-1-decalol; see W. Hückel, R. Dannell, A. Gross and H. Naab, *Ann.*, **502**, 99 (1933), and ref. 12. (c) The present authors wish to acknowledge the contributions of P. B. Sargeant, S. Ranganathan, D. C. Berndt and S.-Y. Lee to these stereochemical conclusions.[13a,b] (d) W. von E. Doering, 139th Meeting of the American Chemical Society, St. Louis, Mo., March 30, 1961.

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SELECTIVE HYDROGENATION OF AN AROMATIC RING IN A NITRO COMPOUND[1]

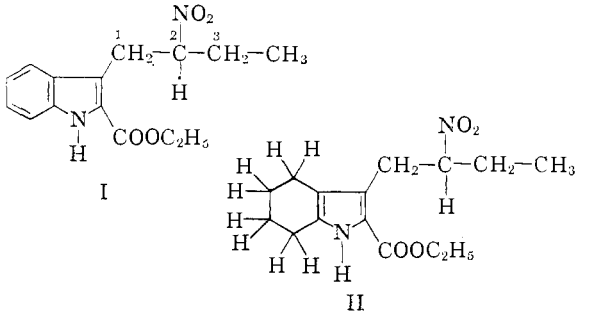
Sir:

We wish to report an instance of the selective hydrogenation of the benzene ring in a compound (I) that also contains a nitro group, the selectivity evidently resulting from a combination of steric and electronic factors that protect the nitro group and facilitate attack on the aromatic system.

(1) Support of this work by a grant (G-6223) from the National Science Foundation is gratefully acknowledged.

Prolonged (72 hr.) catalytic hydrogenation of 1-(α-carbethoxy-β-indolyl)-2-nitrobutane (I) in glacial acetic acid over 30% Pd/C at about 3 atm. and at room temperature led to II (48%), m.p. 122.5–124.5°, $\lambda_{max.}^{95\% \text{ ethanol}}$ 288, 227 (ϵ, 16,240, 6,380), n.m.r., no aromatic protons. *Anal.* Calcd. for $C_{15}H_{22}N_2O_4$: C, 61.20; H, 7.53; N, 9.52; mol. wt., 294.3. Found: C, 61.30; H, 7.40; N, 9.48; mol. wt. (Rast, camphor), 291. When the reaction was repeated in a different hydrogenator with catalyst from a different lot, II was isolated in 50% yield after 50 hr. Some of the Bz-tetrahydroamine (III, about 22%) was isolated in each experiment as the perchlorate, m.p. 232–234° dec., $\lambda_{max.}^{95\% \text{ ethanol}}$ 287, 245 (ϵ, 18,420, 4,240). *Anal.* Calcd. for $C_{15}H_{25}N_2O_6Cl$: C, 49.39; H, 6.91; N, 7.68. Found: C, 49.52; H, 7.17; N, 7.69. Compound I could be regenerated from II by chloranil dehydrogenation. Hydrogenation of 1-(α-carbethoxy-β-indolyl)-2-nitropropane (IV) under essentially the same conditions (except for a shorter time employed because of the more rapid consumption of hydrogen) occurred in normal fashion, producing a mixture of 1-(α-carbethoxy-β-indolyl)-2-aminopropane (V, 46%) and the corresponding lactam, 1-oxo-3-methyl-1,2,3,4-tetrahydropyrido[3,4-b]indole (VI, 13%). The amine (V) was isolated as the perchlorate, m.p. 240.5–241.5° dec.; $\lambda_{max.}^{95\% \text{ ethanol}}$ 296, 228 (ϵ, 21,240, 24,900). *Anal.*, Calcd. for $C_{14}H_{19}N_2O_6Cl$: C, 48.47; H, 5.52; N, 8.08. Found: C, 48.57; H, 5.60; N, 7.77.

Compounds I and IV also were reduced by a chemical method to form the respective lactams (VII) and (VI). Treatment of I with zinc in aqueous acetic acid for 5 hr. at 40° gave VII (41%), m.p. 190–191.5° subl., infrared, lactam carbonyl at 1660 cm.$^{-1}$. *Anal.* Calcd. for $C_{13}H_{14}N_2O$: C, 72.88; H, 6.59; N, 13.08. Found: C, 73.12; H, 6.31; N, 12.92. Similar treatment of IV gave VI (59%), m.p. 226–227° subl., infrared, lactam carbonyl 1660 cm.$^{-1}$. *Anal.* Calcd. for $C_{12}H_{12}N_2O$: C, 71.97; H, 6.04; N, 13.99. Found: C, 71.92; H, 5.94; N, 13.82.



I

II

The slow hydrogenation of the nitro function in I, in contrast to the relatively rapid hydrogenation of that in IV, suggests that the methyl group attached to the 3-carbon atom of I, in conjunction with the steric requirements of the remainder of the molecule I, hinders contact between the nitro function and the catalyst surface. Indeed, an examination of models (Stuart and Briegleb) reveals that the nitro function in both I and IV is in a sterically crowded environment. The fundamental structure of IV, having the carbethoxy group coplanar with the aromatic nucleus (carbonyl infrared absorption of the ester function appears near 1695 cm.$^{-1}$), is such that the nitro group can occupy only a restricted number of positions. Addition of the methyl group to the 3-carbon atom (to give I) blocks the only remaining approach to the close proximity of the nitro group. The observation that hydrogenation of the benzene ring in I occurs when the nitro function is isolated from the catalyst surface further suggests that electron-attraction by the nitro group facilitates hydrogenation of the benzene ring. Several known examples of hydrogenation of the benzene ring of an indole nucleus,[2,3] especially in the field of β-carboline alkaloids,[4,5] support the hypothesis that a more or less remote electron-attracting group may produce such an effect.

(2) V. Boekelheide and Chu-tsin Liu, *J. Am. Chem. Soc.*, **74**, 4920 (1952).

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(4) H. Schwarz and E. Schlittler, *Helv. Chim. Acta*, **34**, 629 (1951), and references therein.

(5) A. LeHir, R. Goutarel and M. M. Janot, *Bull. soc. chim. France*, **19**, 1091 (1952).

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GLUTAMIC ACID DEHYDROGENASE—A PROTEIN OF UNUSUAL CONFORMATION[1]

Sir:

A systematic study of the optical rotatory dispersion of globular proteins showed that about 40% of them have relatively high rotatory dispersion constants (λ_c) of 250–290 mμ, and that all proteins are levorotatory.[2,3,4] Among the enzymes, the slightly levorotatory dehydrogenases exhibit high λ_c values indicating a high α-helix content in these macromolecules.[5,6,7,8] It was, however, most surprising that the glutamic acid dehydrogenase (GAD)[9] was *dextrorotatory*. Upon a mild denaturation with alkali of *p*H 9.5 a negative shift of the rotation was observed, and a λ_c of 316 ($\pm$15) mμ was obtained at the beginning of the alkali treatment. The negative shift could be followed about 4–5 hours after the addition of alkali. At the end of this period the λ_c dropped to 240 mμ, and further observation was impossible because of increasing turbidity of the solution. The data, which were obtained with a Rudolph model 80 photoelectric spectropolarimeter, are shown in Table I.

(1) This study is supported in part by grants from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service, grant C-1785, and the Robert A. Welch Foundation, Houston, Texas, grant G-052.

(2) J. T. Yang and P. Doty, *J. Am. Chem. Soc.*, **79**, 761 (1957).

(3) B. Jirgensons, *Arch. Biochem. Biophys.*, **74**, 57, 70 (1958); **78**, 235 (1958).

(4) J. A. Schellman and Ch. G. Schellman, *J. Polymer Sci.*, **49**, 129 (1961).

(5) B. Jirgensons, *Arch. Biochem. Biophys.*, **85**, 532 (1959); **92**, 216 (1961).

(6) H. Sund, *Biochem. Z.*, **333**, 205 (1960).

(7) B. K. Joyce and S. Grisolia, *J. Biol. Chem.*, **236**, 725 (1961).

(8) D. D. Ulmer and B. L. Vallee, *ibid.*, **236**, 730 (1961).

(9) The GAD preparations were obtained from California Corporation for Biochemical Research, Los Angeles; the crystallized enzyme was isolated from bovine liver by the C. F. Boehringer & Soehne G.m.b.H., Mannheim, Germany. The enzyme was obtained as a suspension of the crystals in either sodium sulfate or ammonium sulfate solutions. The crystals were dissolved by dialysis against dilute solutions of sodium phosphate or sulfate.